

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 99E-1086]

Determination of Regulatory Review Period for Purposes of Patent
Extension; ENBREL

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) has determined the regulatory review period for ENBREL and is publishing this notice of that determination as required by law. FDA has made the determination because of the submission of an application to the Director of Patents and Trademarks, Department of Commerce, for the extension of a patent which claims that human biological product.

ADDRESSES: Submit written comments and petitions to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT:

Claudia Grillo,
Office of Regulatory Policy (HFD-007),
Food and Drug Administration,
5600 Fishers Lane,
Rockville, MD 20857,
301-827-4565.

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Certifier R. LEDFEMA

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SUPPLEMENTARY INFORMATION: The Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98-417) and the Generic Animal Drug and Patent Term Restoration Act (Public Law 100-670) generally provide that a patent may be extended for a period of up to 5 years so long as the patented item (human drug product, animal drug product, medical device, food additive, or color additive) was subject to regulatory review by FDA before the item was marketed. Under these acts, a product's regulatory review period forms the basis for determining the amount of extension an applicant may receive.

A regulatory review period consists of two periods of time: A testing phase and an approval phase. For human biological products, the testing phase begins when the exemption to permit the clinical investigations of the biological becomes effective and runs until the approval phase begins. The approval phase starts with the initial submission of an application to market the human biological product and continues until FDA grants permission to market the biological product. Although only a portion of a regulatory review period may count toward the actual amount of extension that the Commissioner of Patents and Trademarks may award (for example, half the testing phase must be subtracted as well as any time that may have occurred before the patent was issued), FDA's determination of the length of a regulatory review period for a human biological product will

include all of the testing phase and approval phase as specified in 35 U.S.C. 156(g) (1) (B) .

FDA recently approved for marketing the human biological product ENBREL (etanercept). ENBREL is indicated for the reduction in signs and symptoms of moderately to severely active rheumatoid arthritis in patients who have had an inadequate response to one or more disease-modifying antirheumatic drugs. Subsequent to this approval, the Patent and Trademark Office received a patent term restoration application for ENBREL (U.S. Patent No. 5,712,155) from Immunex Corp., and the Patent and Trademark Office requested FDA's assistance in determining this patent's eligibility for patent term restoration. In a letter dated August 7, 2000, FDA advised the Patent and Trademark Office that this human biological product had undergone a regulatory review period and that the approval of ENBREL represented the first permitted commercial marketing or use of the product. Shortly thereafter, the Patent and Trademark Office requested that FDA determine the product's regulatory review period.

FDA has determined that the applicable regulatory review period for ENBREL is 2,322 days. Of this time, 2,143 days occurred during the testing phase of the regulatory review period, while 179 days occurred during the approval phase. These periods of time were derived from the following dates:

1. The date an exemption under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)) became

effective: June 26, 1992. FDA has verified the applicant's claim that the date the investigational new drug application became effective was on June 26, 1992.

2. The date the application was initially submitted with respect to the human biological product under section 351 of the Public Health Service Act: May 8, 1998. The applicant claims March 9, 1998, as the date the product license application (BLA) for ENBREL (BLA 98-0286) was initially submitted. However, FDA records indicate that BLA 98-0286 was submitted on May 8, 1998.

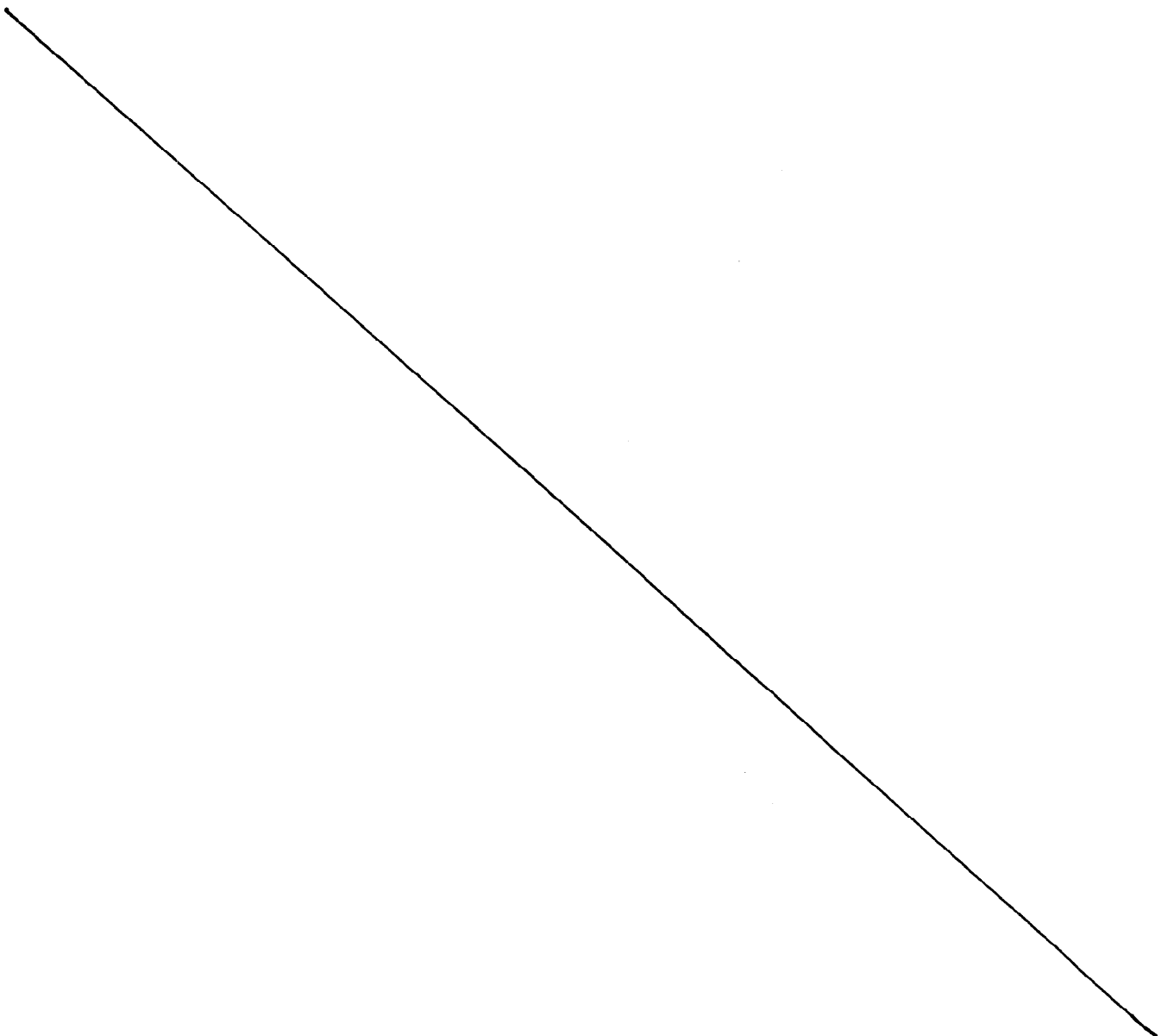
3. The date the application was approved: November 2, 1998. FDA has verified the applicant's claim that BLA 98-0286 was approved on November 2, 1998.

This determination of the regulatory review period establishes the maximum potential length of a patent extension. However, the U.S. Patent and Trademark Office applies several statutory limitations in its calculations of the actual period for patent extension. In its application for patent extension, this applicant seeks 240 days of patent term extension.

Anyone with knowledge that any of the dates as published are incorrect may, on or before [insert date 60 days after date of publication in the FEDERAL REGISTER], submit to the Dockets Management Branch (see ADDRESSES) written comments and ask for a redetermination. Furthermore, any interested person may petition FDA, on or before [insert date 180 days after date of publication in the FEDERAL REGISTER], for a determination regarding whether

the applicant for extension acted with due diligence during the regulatory review period. To meet its burden, the petition must contain sufficient facts to merit an FDA investigation. (See H. Rept. 857, part 1, 98th Cong., 2d sess., pp. 41-42, 1984.) Petitions should be in the format specified in 21 CFR 10.30.

Comments and petitions should be submitted to the Dockets Management Branch. Three copies of any information are to be submitted, except that individuals may submit one copy. Comments are to be identified with the



docket number found in brackets in the heading of this document.

Comments and petitions may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: April 17, 2002.
April 17, 2002.

Jane A. Axelrad
Jane A. Axelrad
Associate Director for Policy
Center for Drug Evaluation and Research

**CERTIFIED TO BE A TRUE
COPY OF THE ORIGINAL**

Regina Sedeno